Message

From: Vulimiri, Suryanarayana [Vulimiri.Sury@epa.gov]
Sent: 11/30/2017 9:57:09 PM
To: Bussard, David [Bussard.David@epa.gov]; Kraft, Andrew [Kraft.Andrew@epa.gov]; Glenn, Barbara [Glenn.Barbara@epa.gov]; Ramasamy, Santhini [Ramasamy.Santhini@epa.gov]; Subramaniam, Ravi [Subramaniam.Ravi@epa.gov]
Subject: RE: Hot off the press on Endogenous Formaldehyde
Attachments: Points from Burgos-Barragan et al 2017.docx

Hi David,

Ex. 5 Deliberative Process (DP)

Let me know if there is something else that needs to be done. I will be happy to do.

Sury

Sury Vulimiri, Ph.D., DABT National Center for Environmental Assessment, Office of Research & Development, US EPA. Phone: 919-541-3558 | Fax: 919-541-0245 | vulimiri.sury@epa.gov

From: Bussard, David
Sent: Thursday, November 30, 2017 9:09 AM
To: Vulimiri, Suryanarayana <Vulimiri.Sury@epa.gov>; Kraft, Andrew <Kraft.Andrew@epa.gov>; Glenn, Barbara <Glenn.Barbara@epa.gov>; Ramasamy, Santhini <Ramasamy.Santhini@epa.gov>; Subramaniam, Ravi <Subramaniam.Ravi@epa.gov>
Subject: RE: Hot off the press on Endogenous Formaldehyde

Sury,

Actually, any chance you can give this more urgency? At least if we think something should be added to the draft assessment? Andrew and Barbara are trying to finish up a draft we can send into Agency review. If they are going to add something this round, they'll need text very soon. And, if the IOAA asks about this paper, we'll need an answer soon.

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

David

From: Vulimiri, Suryanarayana
Sent: Thursday, November 30, 2017 8:48 AM
To: Bussard, David <Bussard.David@epa.gov>; Kraft, Andrew <Kraft.Andrew@epa.gov>; Glenn, Barbara <Glenn.Barbara@epa.gov>; Ramasamy, Santhini <Ramasamy.Santhini@epa.gov>
Subject: RE: Hot off the press on Endogenous Formaldehyde

David,

Ex. 5 Deliberative Process (DP)

Sury

Sury Vulimiri, Ph.D., DABT National Center for Environmental Assessment, Office of Research & Development, US EPA.
Phone: 919-541-3558 | Fax: 919-541-0245 | vulimiri.sury@epa.gov

From: Bussard, David
Sent: Wednesday, November 29, 2017 5:54 PM
To: Kraft, Andrew <Kraft.Andrew@epa.gov>; Glenn, Barbara <Glenn.Barbara@epa.gov>; Ramasamy, Santhini <Ramasamy.Santhini@epa.gov>; Vulimiri, Suryanarayana <Vulimiri.Sury@epa.gov>
Subject: Fwd: Hot off the press on Endogenous Formaldehyde

Thanks Sury.

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

David Bussard

Begin forwarded message:

From: "Vulimiri, Suryanarayana" <Vulimiri.Sury@epa.gov>
Date: November 29, 2017 at 5:39:41 PM EST
To: "Bussard, David" <Bussard.David@epa.gov>
Subject: RE: Hot off the press on Endogenous Formaldehyde

David, that is the question I have. It needs some collective thinking into it. Here are some preliminary thoughts.

Ex. 5 Deliberative Process (DP)

Sury

Sury Vulimiri, Ph.D., DABT National Center for Environmental Assessment, Office of Research & Development, US EPA. Phone: 919-541-3558 | Fax: 919-541-0245 | vulimiri.sury@epa.gov

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From: Bussard, David
Sent: Wednesday, November 29, 2017 5:06 PM
To: Vulimiri, Suryanarayana <Vulimiri.Sury@epa.gov>
Subject: RE: Hot off the press on Endogenous Formaldehyde

Thanks Sury

Ex. 5 Deliberative Process (DP)

David

From: Vulimiri, Suryanarayana
Sent: Wednesday, November 29, 2017 4:43 PM
To: Bateson, Thomas <Bateson.Thomas@epa.gov>; Glenn, Barbara <Glenn.Barbara@epa.gov>; Fritz, Jason <Fritz.Jason@epa.gov>; Kraft, Andrew <Kraft.Andrew@epa.gov>; Makris, Susan <Makris.Susan@epa.gov>; Segal, Deborah <Segal.Deborah@epa.gov>; Subramaniam, Ravi <Subramaniam.Ravi@epa.gov>; Vulimiri, Suryanarayana <Vulimiri.Sury@epa.gov>; Whalan, John <Whalan.John@epa.gov>
Cc: Bussard, David <Bussard.David@epa.gov>; Ramasamy, Santhini <Ramasamy.Santhini@epa.gov>
Subject: Hot off the press on Endogenous Formaldehyde

Nature. 2017 Aug 31;548(7669):549-554. doi: 10.1038/nature23481. Epub 2017 Aug 16.

Mammals divert endogenous genotoxic formaldehyde into one-carbon metabolism.

Burgos-Barragan G[1], Wit N[1], Meiser J[2], Dingler FA[1], Pietzke M[2], Mulderrig L[1], Pontel LB[1], Rosado IV[3], Brewer TF[4], Cordell RL[5], Monks PS[5], Chang CJ[4], Vazquez A[2], Patel KJ[1,6].

Author information

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Abstract

The folate-driven one-carbon (1C) cycle is a fundamental metabolic hub in cells that enables the synthesis of nucleotides and amino acids and epigenetic modifications. This cycle might also release formaldehyde, a potent protein and DNA crosslinking agent that organisms produce in substantial quantities. Here we show that supplementation with tetrahydrofolate, the essential cofactor of this cycle, and other oxidation-prone folate derivatives kills human, mouse and chicken cells that cannot detoxify formaldehyde or that lack DNA crosslink repair. Notably, formaldehyde is generated from oxidative decomposition of the folate backbone. Furthermore, we find that formaldehyde detoxification in human cells generates formate, and thereby promotes nucleotide synthesis. This supply of 1C units is sufficient to sustain the growth of cells that are

unable to use serine, which is the predominant source of 1C units. These findings identify an unexpected source of formaldehyde and, more generally, indicate that the detoxification of this ubiquitous endogenous genotoxin creates a benign 1C unit that can sustain essential metabolism.

PMID:
28813411
DOI:
10.1038/nature23481

<< File: Burgos-Barragan et al 2017_EndogenouFA.pdf >> << File: Pontel et al 2015_SV.pdf >>
So the bottom line is that endogenous formaldehyde is safely handled by the cells diverting it into normal cellular metabolism. This is published in Nature (PDF attached).

Ex. 5 Deliberative Process (DP)

Sury

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